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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Desnoyers, et al.
Appl. No. : 10/036,041
Filed : December 26, 2001
For : NOVEL NUCLEIC ACIDS
ENCODING PEPTIDES THAT
INDUCE CHONDROCYTE
REDIFFERENTIATION
Examiner : Jiang, Dong
Group Art Unit : 1646

DECLARATION OF LUC DESNOYERS AND WILLIAM I. WOOD
UNDER 37 CFR §1.131

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

We, Luc Desnoyers and William I. Wood, declare and state as follows:

1. We are the inventors of the subject matter that is presently claimed in the above-captioned patent application.
2. During the time period in which all of the events and activities described herein occurred, we were employed by Genentech, Inc., the assignee of the above-captioned application.
3. All of the events and activities described herein were performed by us personally, or under our direction, as part of our duties as employees of Genentech, Inc.
4. The invention claimed in the above-captioned patent application was conceived prior to April 20, 1999 and diligently reduced to practice thereafter in the U.S. as described below.
5. Prior to April 20, 1999, we conceived of the nucleic acid sequences claimed in the above-captioned patent application. This is demonstrated by the attached sequence printout (Exhibit A), which was generated prior to April 20, 1999, and which shows the complete sequence of the nucleic acid having the sequence of SEQ ID NO:1. The attached printout also shows the complete sequence of the polypeptide which has the sequence of SEQ ID NO:2. As evidenced by the sequence printout, we were in possession of the complete nucleic acid sequence prior to April 20, 1999.
6. The date deleted from page 1 of Exhibit A is a date prior to April 20, 1999, and was redacted pursuant to M.P.E.P. § 715.07. The redacted date is the date when the data were generated; the date the report was printed, April 16, 2004, remains on the report.

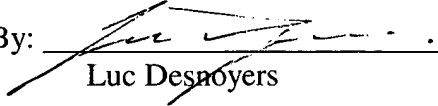
Appl. No. : 10/036,041
Filed : December 26, 2001

7. After initially conceiving the nucleic acid having the sequence of SEQ ID NO:1 prior to April 20, 1999, we diligently reduced the claimed subject matter to practice by working to express and purify the encoded polypeptide and to run it systematically through many assays. The cDNA was deposited with the American Type Culture Collection (ATCC) on January 12, 1999 and assigned ATCC no. 203581. The protein of interest was assigned a "protein inventory number" (e.g., PIN1308 and PIN1308-1). As set forth in the enclosed Exhibit B, the polypeptide was expressed in *E. coli* - PUR1009 (see page 2) on November 16, 1998; in *Baculovirus* - PUR1039 (see page 3) on November 23, 1998; and in mammalian cells (see page 4) on February 17, 1999. Furthermore, various constructs with poly-His or IgG tags were made from the time of first cloning and construction of these was followed by expression and purification of the encoded protein during the time period of prior to April 20, 1999 through March 13, 2003. For example, Exhibit C shows July 13, 1999 as the date of purification of a polypeptide having the sequence of SEQ ID NO:2. PIN1308 and/or PIN1308-1 were distributed to various scientists for multiple cell-based assays and/or quality confirmation tests from August 20, 1999 through January 22, 2001.

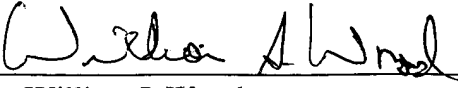
8. Exhibits D and E list the assays performed on the purified protein. Assay ASY110, called "Chondrocyte Re-differentiation Assay" was completed on November 10, 1999 for PIN1308-1, which is a polypeptide encoded by a nucleic acid having the sequence of SEQ ID NO:1. PIN1308-1 was delivered to Luc Desnoyers for one of the assay runs on October 22, 1999; testing was completed on November 10, 1999. Exhibit E is an assay result list that shows positive results for the assay completed on November 10, 1999, thereby confirming the ability of the encoded polypeptide to induce chondrocyte redifferentiation. Thus, actual reduction to practice occurred at least by November 10, 1999.

9. After reducing the invention to practice, we worked with the Genentech, Inc. patent department to prepare a non-provisional patent application, which included the sequence of SEQ ID NO:2, as well as the data showing the ability to induce chondrocyte redifferentiation. That application was filed on March 1, 2000.

10. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

By: 
Luc Desnoyers

Date: 05/17/2004

By: 
William I. Wood

Date: 5/17/04

Appl. No. : **10/036,041**
Filed : **December 26, 2001**

EXHIBIT A

(16 pages; pages 4-19)

EXHIBIT A—PAGE 1

>Friday, April 16, 2004
 >DNA44686 [Full]
 >564 Sites [All Sites]
 >
 >Sequence confirmed by phrap.

[DNA44686, sheldens

```

rmaI
sau3AI kaeI
mboI/ndeII[dam-]
dpmI-[dam-]
dpmI'(dam+)
alwI(dam-) sau3AI
nlaIV xbaI mboI/nde-I[dam-]
haeIII/palI b'fai dpmII[dam-]
mwoI haeIII/palI b'fai dpmII[dam-]
bglII(M.haeIII-) hpy88III taqI
tfil apoI sfil eaeI bstVI/xhoII dpmI(dam+)
hinfI(M.taqI-) cfrI bamHI(M.mspI-) mnlI
taqI(M.claI-) haeIII/palI alwI(dam-) alwI(dam-)
cla-/bsp106 eaeI bsrI mspI(M.bamHI-)(M.haeIII-) taqI
bspDI(dam-) cfrI tepRI hpaII mnlI bstVI/xhoII mnlI drdI aflIII bssKI avai bs
bsgl bsaJI bspDI(dam-) TCGGCCACAC TGGCCGAT CTTGAGAT CCTCGACCT CGACCCAGC GTCCGGCAT CTGCCGAGG
1 CAACITGCACC TCGCTTCTA CGATTCGAT TCGGCCACAC TGGCCGAT CTTGAGAT CCTCGACCT CGACCCAGC GTCCGGCAT CTGCCGAGG
CTTGACGTGG AGCCAGATA GCTAAGCTTA AGCCGGTGTG ACCGGCCTAG GAGATCTCTA GGGAGCTGA CAGGCCGCTC GACGGGCTCC
insert starts here

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GSeqEdit, DNA44686 [Full], page 1

EXHIBIT A—PAGE 2

```

sstI
sacI
hg-AI/aspHI [M.aluI-]
ec1136I-
bsp1286 [M.aluI-]
bsiHKA1
bmy-
banII [M.aluI-]
scrFI [dcn-]
pspGI
mvaI aluI
ecorII [dcn-]
daav [dcn-]
bstNI mboII pleI ddeI
bsaKI [dcn-] opaI mlyI bspCNI
mwoI bpaZ/gsuI [dcn-] ddeI hinfI mnlI
bstXI apyI [dcn+] bbsI bspCNI bsmAI hpy188I hinfI mwoI mnlI aluI czc8I
101 AGACCAAGCT CCGTGGAGCTC TCGTGTCTTC TCGGGAGAC TCTGAGGCTC CGTGGAGAT CATGCTTGG AGGCAGCTCA TCTATGGCA AC1GCTGGCT
TCTGGTGGGA GGACCTCGAG ACGACAGAAG AGTCCCTCTG AGACTCCGAG ACAACTCTTA GTACGAAPCC TCCGTGGAGT AGATACCGT TGACGACCGA
N L W R Q L I Y W Q L L A
^MET

pleI mnlI
mlyI mspI hpyCHAV
hinfI bslI hpaII sfcI bsmAI
hpy188II nlaII bsmAI bsaNI pstI nlaII sfc
201 CTGTTTTCCTTCC TCCCTTTTCTG CCGTGTGICAA GATGATACA TGGAGTCTCC ACAACCGGA GGACTACCCC CAGACTGCCAG TAAGTGTGT CATGGAGACT
AACAAAAGG AGGGAAGAC GGACACAGTT CTACTATCT CTACTATCT ACCTCAGAGG TGT11GGCTT CCTGATGGGG GTCTGACGTC ATTCAACACA GTACCTCTGA
14 L ? F L ? F C L C Q D E Y M E S P Q T G G L P P D C S K C C H G D Y

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GSeqEdit, DNA44686 (Full), page 2

EXHIBIT A—PAGE 3

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mwol
  bglI[M.haeIII-]
  sau96I[N.haeIII-]
  sau96I[M.haeIII-]
  pspOMI/bspI20I
  nlaIV scrFI[dcM-]
    sau96I[dcM-][M.haeIII-]
    scrFI[dcM-] eco0109I/draII scrFI[dcM-]
    pspGI scrFI[M.hpall-] pspGI
    mval nciI pspGI mval nlaIII
    ecoRII[dcM-] haeIII/pall ecoRII[dcM-]
    dsav[dcM-] bspI286[M.haeIII-] xcmI
    ostNI mspI mval dsav[dcM-]
    bssKI[dcM-] bmyI ecoRII[dcM-] styI
    bsaJI hpall dsav[dcM-] ncoI
    sau96I[M.haeIII-] banII[M.haeIII-] bstNI dsal
    xcmI n-laIV apy-[dcM-] apaI bstNI bssKI[dcM-]
    styI haeIII/pa-I dsav bssKI[dcM-] btgI/bstDSI
    mwol mnlI bsaJI bsaJ- haeIII/pall apyI[dcM+] bsaJI
    aluI taqI mwol ecc0109I/draII bssKI mnlI bsmI apyI[dcM+]
    301 ACAGCTTTCG AGGCTACCAA GGCCTCCCTG GGCACCCGGG CCGCTCTGCG ATTCAGGAA ACCATGGAAC CAATGCGAAC AATGAGCCA CTGGTCATGA
    TGTGGAAGC CCCGAIGETT CCGSGGGGAC CCGSTGGGCC GGGAGGACCG TAGGTCTCTT TGTACCTTT GTTACCGTTG TTACTCGGT GACCACTACT
    4E S F R G Y Q G P P G P P G P F G I P G N H G N N G N N G A T G H E
  
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GSeqEdit, DRA44686 [Full], page 4

GSeqEdit, DNA44686 [Full], page 5

EXHIBIT A—PAGE 6

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nlaIII
styI
ncoI sau96I
dsal nlaIV
tseI          hinPI          btgI/bstOSI          tfII
fokI          fnu4HI/bsoFI          hhaI/cfoI          bsmFI          h-nfI
bstf5I        bbvI          bsrDI haeII          bsajI avall          hpyCH4V          ddeI
801 AAPAGGGGATG AGGTTTGGCT GCGAATGGGC AATGGGCTC TCCATGGGA CCACCAACGC TTCTCCACCT TTGCAAGATT CCTGCCTCTT GAAACTAAGT
TTTCCCTTAC TCCAAACCGA CGCTTACCG TTACCGCGAG AGGTACCCCT GGTGGTTGCG AGRAGGTGGA AACGTCTTA GSACGAGAA CTTTGATTCA
214 K G D E V N L R M G N G A L H G D H Q R F S T F A G F L L F E T K O

mnlI
ddeI
bspCN1
sau3AI
mboI/ndeII[dam-]
dpmII{dam-}
dpmI{dam+}          tru9I
maeII hpy188I          mseI          mnlI          bsrD:
90: AAATATATGA CTAGATAGC TCCACTTGG GGAAGACTTG TAGCTAGCT GATTGTATC GATCTGAGG ACATTAAGT TGRGGGTTT ACATGCTCT
TATATATCT GATCTATCG AGGTGAACCC CCTTCTGAC CTAAACATG CTAGACTCTT TGTATTTCA ACTCCCAAA TGTACGACA

ddeI
bsp1286          tfII          dd
bmyI hpy188I          mboII
banII mboII          bpuAI          bbsI bs
tsp509:          bsrDI          hpyCH4V          bspCN1 hinf:
tsp509:          hpyCH4V          sfcI          csp6I          bbsI bs
100: ACTCAAAA TTATTGGTG CAATGTGTC CACGCTACAG GTACACCAAT AATGTTGGAC AATTCAGGG CTCAGAGAA TCAACCAAA AATAGTCTTC
TAAGTTCTT AATACCAAC GTTACACAA GCGGCTGTC CAATGGTTA TTACACCTG TTAAGTCCC GAGTCTCTT AGTTGTTCT TATCAGAG

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GSeqEdit, DNA44686 [Full], page 6

EXHIBIT A—PAGE 7

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nlaIV      nlaIV      nlaIV      nlaIV      nlaIV      nlaIV      nlaIV      nlaIV      nlaIV      nlaIV
banI      banI      banI      banI      banI      banI      banI      banI      banI      banI
styi      styI      styI      styI      styI      styI      styI      styI      styI      styI
bsaJI      bsaJI      bsaJI      bsaJI      bsaJI      bsaJI      bsaJI      bsaJI      bsaJI      bsaJI
tsp509I    tsp509I    tsp509I    tsp509I    tsp509I    tsp509I    tsp509I    tsp509I    tsp509I    tsp509I
sspI      sspI      sspI      sspI      sspI      sspI      sspI      sspI      sspI      sspI
1101 TCAGATGACC TTGACTAATA TACTCAGCAT CTTTACACT CTTTCTCTGG CACTTAAAG ATAAATTCCTC TCTGACGCAG GTTGGAAATA TTTTWTCTTA
ACCTTACTGS AACTGATTAT ACAGAGCCTA GAAATAGTGA GAAAGGACCC GTGGATTTTC TATTAGAGG AGACTCCCTC CACCTTAT AAATAAGAC
apoI      apoI      apoI      apoI      apoI      apoI      apoI      apoI      apoI      apoI
trp509I    trp509I    trp509I    trp509I    trp509I    trp509I    trp509I    trp509I    trp509I    trp509I
trp509I    trp509I    trp509I    trp509I    trp509I    trp509I    trp509I    trp509I    trp509I    trp509I
1201 TCACAGAGT CATTTCGAA GAAATTCGAC TACTCTGCTT TTAATTTAAT ACCAGTTTC AGGACCCCT GAAGTTTAA GTTCAATATT CTTTATAACA
AGTGTCTCTA GTAAAGCTTT CTTAATCTG ATGAGACGAA AATTAATTA TGGTCAAGAG TCCTTGGGA CTTCAAAAT CAAGTATATA GAATATTTGT
tseI      tseI      tseI      tseI      tseI      tseI      tseI      tseI      tseI      tseI
fnu4HI/bsoFI
maeI      maeI      maeI      maeI      maeI      maeI      maeI      maeI      maeI      maeI
mwoI      mwoI      mwoI      mwoI      mwoI      mwoI      mwoI      mwoI      mwoI      mwoI
bbvI      bbvI      bbvI      bbvI      bbvI      bbvI      bbvI      bbvI      bbvI      bbvI
bstAPI     bstAPI     bstAPI     bstAPI     bstAPI     bstAPI     bstAPI     bstAPI     bstAPI     bstAPI
bsp1286    bsp1286    bsp1286    bsp1286    bsp1286    bsp1286    bsp1286    bsp1286    bsp1286    bsp1286
bmyI      bmyI      bmyI      bmyI      bmyI      bmyI      bmyI      bmyI      bmyI      bmyI
bfaI      bfaI      bfaI      bfaI      bfaI      bfaI      bfaI      bfaI      bfaI      bfaI
mvoI      mvoI      mvoI      mvoI      mvoI      mvoI      mvoI      mvoI      mvoI      mvoI
alul      alul      alul      alul      alul      alul      alul      alul      alul      alul
tsp509I    tsp509I    tsp509I    tsp509I    tsp509I    tsp509I    tsp509I    tsp509I    tsp509I    tsp509I
mnlI      mnlI      mnlI      mnlI      mnlI      mnlI      mnlI      mnlI      mnlI      mnlI
1301 TTTCAGAGAA TCGGATCTAG TGATAAGACA GGGCTGGGGC AAGACAGGG GCATAGCTG CCTTATPAG TAAATTAGTG CCTCCCTGT TCAGCTTAGC
AACTCTCTI AGCCATCATC ACTATPACTGT CCGAGCCCG TTCTTGTCCTC CGTATCGAC GGAATATCG ATTAATCAC GGGAGGCACA AGTCGAATCG

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EXHIBIT A—PAGE 8

sau3AI
 mboI/ndeI-[dam-]
 dpnI-[dar-]
 dpnI-[dan+]
 alwI-[dan-]
 1401 CTTTCACCT TTCTTTTGA TCCACAAAT ACATTAAAC TCTGAATTCA CATACATGC TAITTTAAG TCAATAGATT TTAGCTATAA RGTGCTTGAC
 GAADCTGGGA AAGGAACI AGGTCTTTA TGTATTTTG AGACTTAAGT GTATGTACG ATAAAATTC AGTTATCTAA AATCGATATT TCACGACGTG
 foki
 bstF5I
 mnlI
 trn9I
 mseI
 aha-II/craI
 aluI
 bs
 bs
 150: CAGTAATGIG GTTGAATT TTGTAGTGT CCCCACATC GCCCCCAACT TCGGATGTGG GGTGAGGAGG TTGAGGTTCA CTATTACAA ATGTCATAPA
 CTCATTACAC CAACATIAA ACACATACAA GGGGGTGTAG CGGGGGTTGA AGCTACACC CCAGTCTCTCC AACTCCAGGT GATAATGTT TACAGTATT
 hincII/hindII
 nlaIII
 nspHI
 nspI
 hpyCH4V
 mnlI
 hpy188I
 eco57I
 mbcII
 trn9I
 mseI
 dde-
 aseI/asnI/vspI
 1601 TATCTCATG AGGTACAGT CCAATAGATA TTCAAATGTT GCATGTGAC CAGAGGAGT TTATATCTGA AGACATACA CTATTAAIAA ATACCTTAGA
 ACACAGTATC TCCATGTAC GGTTACTAT AAGTTTACA CGTACACTG GTCTCCCTAA AATAGACI TCTTGTATGT GATAATATT TATGCAATCT

190- ATAFEG
TAFIAC

EXHIBIT A—PAGE 10

```

> length: 1986

accI (GTNKAAC) :
acII (CGGC) :
aflIII (ACRYGT) :
ahaiII (TTYAA) :
alul (AGCT) :
a_wI (GCATCNRN) :
apaI (GGCCC) :
apoI (RANTY) :
apyI (CONGG) :
aseI (ATTAAT) :
asnI (ATTAAT) :
aspEI (GWCWC) :
avaI (CYCGG) :
avaII (GWC) :
banHI (GGATCC) :
batI (GGYACC) :
banII (GRGTC) :
bbsI (GAAGACNNNNN) :
bbvI (GCACC) :
b_sai (CTAG) :
bglI (GCCNNNNNGGC) :
blpI (GCTNAGC) :
bmyI (GGGCHC) :
bpuI (CTGGAG) :
bpu1102I (GCTNAGC) :
bpuAI (GAAGACNNNNKY) :

1832
452 1815 1819 :870
77
1464
116 175 303 741 793 918 942 947 1354 1368 1393 1483 1863 1896
46 47 58 1419
338 628
27 1221 1444
111 327 345 354 434 1713
1683
1683
115
94 442 488
848
46
1149
115 338 628 1068
125 726 932 1095
173 458 818 1357 1894
53 795 911 1354 1827
34 340 1869
943 :394
:15 338 628 1368 1349 1378
:12
943 1394
125 726 932 1095

GSeqEdit, DNA4686 [Full], page 10

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EXHIBIT A—PAGE 11

bsaI (GGTCTCRNNNN) : 100 582
 bsaj (CCNNGG) : 9 95 317 326 327 362 434 488 489 842 1145 1873
 bsaW (NCCGGSW) : 255
 bse3I (GAGGAGNNNNNNNN) : 97 1167
 bsgI (GTGCAG) : 4
 bel1236I (CGCG) : 78 1820
 bsiCI (TTCGAA) : 24
 bsiEI (CGRYCG) : 1816
 bsiHKAI (GNGCWC) : 115
 bali (CCNNNNNNNGG) : 249 633 922 1544 1837
 bsmA (GTCTC) : 100 136 245 295 582
 bsmAI (GTCTC) : 100 136 245 295 582
 bsmFI (GGGACNNNNNNNNNN) : 847
 bsm (GAATGON) : 349 516
 bsoFI (GCNGC) : 173 458 818 1357 1815 1818 1869 1894
 bsp106 (ATCGAT) : 19
 bsp120I (GGGCC) : 338 628
 bsp1286 (GDGCHC) : 115 338 628 1068 1349 1378
 bsp1407I (TGTACA) : 736
 bspCN (CTCAGNNNNNNNN) : 130 142 944 964 1071 1100 1123
 bspDI (ATCGAT) : 19
 bspHI (TCATGA) : 395 610
 bspK (ACCTGC) : 1177 1836
 bsrBI (GAGCGG) : 450
 bsrDI (GCAATGNN) : 829 992 1020
 bsrGI (TGTACA) : 736
 bsrI (ACTGGN) : 39 390 615 633 1252 1500
 bask (CCNGG) : 83 111 327 336 345 354 434 488 489 1713
 bst4CI (ACNGI) : 556 723 1615 1729
 bstAPI (GCANNNNTEGC) : 1351

GSeqEdit, DNA44686 [Full], page 11

EXHIBIT A—PAGE 12

bsfBI (ITCGAA) :	24
bslDSI (CCRYGG) :	362 842 1873
bs-EII (GGTNACC) :	429
bstF5I (GGATG) :	680 769 806 1313 1553
bstNI (CCWGG) :	111 327 345 354 434 1713
bstUI (CGCG) :	78 1820
bstXI (CCANNNNTGG) :	104 1500
bs-YI (RGATCX) :	46 57
btgI (CCRYGG) :	362 842 1873
bteI (GCAGTGN) :	574
cac8I (CCNNGC) :	194 794
celII (GCTNACC) :	943 1394
cfoI (GCCTC) :	835
cfrI (YGCCCR) :	32 41 1816 1867
clal (ATCGAT) :	19
csp6I (GTAC) :	701 737 1041 1613
ddeI (CTNAG) :	130 142 895 344 964 1071 1100 1123 1395 1695
dpnI (GATC) :	47 58 961 1419
dpnII (GATC) :	47 58 961 1419
dral (TTTAAA) :	1464
dralI (RGNCCT) :	320 338 437 627 628
drcI (GACNNNNNGTC) :	72 1823
dsaI (CCRYGG) :	362 842 1873
dsav (CCNGC) :	83 111 327 336 345 354 434 488 489 1713
eaeI (YGCCCR) :	32 41 1816 1867
eagI (CGCCCG) :	1816
ec1136II (GAGCTC) :	115
ec-X (CGCCCG) :	1816
eco57I (CTGAG) :	507 542 569 659 728 789 1269 1667
ecoNI (CTNNNNNAG) :	1837

GSeqEdit, DNA44686 [Full], page 12

EXHIBIT C—PAGE 13

eco0109I (RGGNCCY) :	320 338 437 627 628
ecoRI (GAATTC) :	27 1444
ecoRI- (CONEG) :	111 327 345 354 434 1713
esp- (GCTNAGC) :	943 1394
fru4HI (CCNGC) :	173 458 818 1357 1815 1818 1869 1894
fru2II (CGCG) :	78 1820
foxI (GGATG) :	680 769 806 1313 1553
gsvI (CTGGAG) :	112
haeII (RGCGCY) :	834
haeIII (GGCC) :	35 42 321 331 339 439 465 629 1817 1868 1877
hgaI (GACGC) :	79 1174
hgiAI (GNGCWC) :	115
hhaI (GCGC) :	835
h-nPI (GCGC) :	835
hincII (GTYRAC) :	1645 1832
hind-I (GTYRAC) :	1645 1832
hirdIII (AAGCTT) :	1862
hirfi (GATTC) :	22 138 157 243 494 877 1078 1308 1823 1830
hpaII (CGG) :	44 83 256 336 489
hpaI (GCTGA) :	411 429 655
hpy188I (TCNCA) :	141 509 551 762 963 1072 1101 1171 1311 1441 1551 1666
hpy188III (TCNNGA) :	52 227 395 610 1259 1563 1826
hpyCHAII- (ACNCT) :	556 723 1615 1729
hpyCH-V (TCCA) :	5 276 515 709 872 1019 1215 1640 1839 1893
mae- (CTAG) :	53 795 911 1354 1827
maeIII (GTNAC) :	430 956
nboI (GATC) :	47 58 961 1419
nboI- (GAAGA) :	126 568 652 727 932 1075 1096 1669
ncrI (CGRYCC) :	1816
nlwI (ACGGT) :	77

GSeqEdit, DNA44686 [Full], page 13

EXHIBIT C—PAGE 14

hly- (GAGTCNNNNN) :	138 243 1823 1830
hli (CCTC) :	9 50 62 68 97 144 170 209 259 310 342 441 445 678 687 810 966 982
hseI (TTAA) :	1169 1382 1567 1573 1610 1653
hslI (CAYNNKRTG) :	974 1241 1246 1277 1434 1465 1584 1684 1781
hspI (CCGG) :	675
hva- (CCWGG) :	44 83 256 336 489
hvnI (CGCG) :	111 327 345 354 434 1713
hnoI (SCYNNNNNCC) :	78 1820
hclI (CCSGG) :	34 198 164 304 313 340 452 516 525 733 1351 1360 1869
hcoI (CCATGG) :	83 336 488 489
hdelI (GATC) :	362 842 1873
hhe- (GCTAGC) :	47 58 961 1419
h-aiiI (CATG) :	794
hlaIV (GGNNCC) :	161 239 291 363 396 462 521 611 665 675 734 780 843 1642 1874
hoci (CGCGCGC) :	46 321 338 384 402 437 465 627 628 629 847 1149 1262
hspH- (RCATGY) :	1815
hspI (RCATGY) :	733 1641
hser7I (CTCGAG) :	733 1641
h-aiI (GGCC) :	442
hleI (GAGTCNNNN) :	33 42 321 331 339 439 465 629 1817 1868 1877
hslI (TTATAA) :	138 243 1823 1830
hspAI (CCCGGG) :	1293 1899
hpgI (CWGC) :	468
hspOMI (GGGCCC) :	111 327 345 354 434 1713
h-aiI (CTGCAG) :	338 628
hcal (TCAAGA) :	275 1838
h-aiI (CTAG) :	395 610
h-aiI (GTAC) :	53 795 911 1354 1627
hac- (GAGCTC) :	701 737 1041 1613
	115

GSeqEdit, DNA44686 [Full], page 14

EXHIBIT C—PAGE 15

```

sali (GTCGAC) : 1832
sau3AI (GATC) : 47 58 961 1419
sau36I (GCNCC) : 321 330 338 339 438 465 628 629 848 1877
seeI (TAGGGATACAGGGTAAT) : 1844
scrFI (CNGG) : 83 111 327 336 345 354 434 488 489 1713
sfaNI (GCA7C) : 87 1127
sfci (CTRYAG) : 275 299 1035 1838
sfii (GGCCNNNNNGGCC) : 33 1868
sfuI (TTCGAA) : 24
smaI (CCCGGG) : 488
smI (CTYRAG) : 442
sspI (AATATT) : 1187
sstI (GAGCTC) : 115
styI (CCWGG) : 317 362 842 1145 1873
taqI (TCGA) : 20 25 64 70 308 443 1833
tfil (GATC) : 22 157 494 877 1078 1308
thaI (CGCG) : 78 1820
tliI (CTCGAG) : 442
trt9 (TTAA) : 974 1241 1246 1277 1434 1465 1584 1684 1781
tseI (GCGC) : 173 458 818 1357 1894
tsp45I (GTSAC) : 430
tsp509I (AATT) : 28 1009 1061 1163 1222 1243 1372 1445 1516
tspRI (NNCAGTGNN) : 38 389 557 575 1616
vapI (ATTAAT) : 1683
xbaI (TCTAGA) : 52 1826
xcmI (CCANNNNNNNTTGG) : 317 362
xhoI (CTCGAG) : 442
xhoII (RGATCY) : 46 57
xbaI (CCCGGG) : 488
xmaII (CGGCGC) : 1816

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GSeqEdit, DNA44686 [Full], page 15

GSeqEdit, DNA44686 [Full], page 16

Appl. No. : **10/036,041**
Filed : **December 26, 2001**

EXHIBIT B

(4 pages; page 21-24)

Appl. No. : 10/036,041
 Filed : December 26, 2001

EXHIBIT B—PAGE 1

Protein Request FILED

NEW REQUEST SEARCH PRODUCTION HISTORY

PRODUCTION HISTORY UNQ 753 SEARCH

UNQ/53 Human CTRP3 Poly-His

	Order Protein	TransFac DNA	Exp System	Formal Name	PRO	Protein Request	EXP	PUR	PUR Status	PUR Warning	Culture Vols
1.	Order	DNA84665	E Coli	Human CTRP3 Poly-His	PRO1825		EXP2247	PUR1009	Done		
2.	Order	DNA84665	E Coli	Human CTRP3 Poly-His	PRO1825		EXP2247	PUR4414	Done		
3.	Order	DNA87982	Baculovirus	Human CTRP3 IgG	PRO1855		EXP2255	PUR1039	Drop		1
4.	Order	DNA102368	Mammalian Stable	Human CTRP3 Poly-His	PRO4365		EXP2794				

Appl. No. : 10/036,041
 Filed : December 26, 2001

EXHIBIT B—PAGE 2

GENE GENES		SITE MAP		Additional f																	
GENE VIEWER	GENE	FAM	MAP	GENEUB																	
SEQUENCE VIEWER	DNA	SRC	RNA	LIB	FLA																
ASSAY VIEWER	PRO	DOM	EXP	PUR	LOT																
				SELECT	Go																
EXP2247																					
VIEW DNA																					
View F. Mem. P.																					
Update Record																					
Gene Info	UNQ753 PRO 1825 Human CTRP3 Poly-His TFDNA84665 FLDNA44686																				
EXP Lab Name																					
DNA Lab Name	pE44686-1																				
Protein Request ID																					
System	E Coli																				
Expctd. Harvest Date																					
Control																					
Fermentation Run ID																					
Cell Line																					
Expression Media																					
Growth Factors																					
Supplements																					
Warning																					
Gels																					
Expressed	FALSE																				
Comments																					
Status																					
Date Entered	November 9, 1998																				
Date Canceled																					
Scientist	Dan Yansura																				
Notebook	0 -																				
Protein Lots	<table border="1"> <thead> <tr> <th>PUR(s)</th> <th></th> </tr> </thead> <tbody> <tr> <td>PUR1009</td> <td>11/16/98</td> </tr> <tr> <td>PUR4414</td> <td>11/16/01</td> </tr> </tbody> </table>					PUR(s)		PUR1009	11/16/98	PUR4414	11/16/01										
PUR(s)																					
PUR1009	11/16/98																				
PUR4414	11/16/01																				
<table border="1"> <thead> <tr> <th>Harvest Date</th> <th>Cell Pellet</th> <th>Cell Banking ID</th> <th>E Coli Strain</th> <th>Days Incubated</th> <th>Transfection Date</th> <th>Transfer Date</th> <th>Transfer Volume</th> </tr> </thead> <tbody> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </tbody> </table>						Harvest Date	Cell Pellet	Cell Banking ID	E Coli Strain	Days Incubated	Transfection Date	Transfer Date	Transfer Volume								
Harvest Date	Cell Pellet	Cell Banking ID	E Coli Strain	Days Incubated	Transfection Date	Transfer Date	Transfer Volume														
LOT2552 PIN1308-1																					
ASSY DNA DOM EXP FAM FLS LIB LOT MAP OLI PRB PRO PUR RNA SRC UNQ XPT YST Assay Viewer Sequence Viewer Gene Viewer GenesGenes SAGE																					
GenesGenes Feedback																					

Appl. No. : 10/036,041
 Filed : December 26, 2001

EXHIBIT B—PAGE 3

GENE GENES		SITEMAP		Additional F	
GENE VIEWER GENE FAM MAP GENEHUB SEQUENCE VIEWER DNA SRC RNA LIB FLS OLI ASSAY VIEWER PRO DOM EXP PUR LOT ASY		<input type="radio"/> Edit <input type="radio"/> New <input type="radio"/> Update SELECT <input type="text"/> GO			
EXP2255		VIEW DETAILS		VIEW PROFILE	
Gene Info		UNQ753 PRO 1855 Human CTRP3 IgG TFDNA87982 FLDNA44686			
EXP Lab Name		44686.221 JSF			
DNA Lab Name		44686.221JSF Hit			
Protein Request ID					
System		Baculovirus			
Virus Status					
Export Virus Harvest Date		Virus Harvest Date			
Export Harvest Date		Harvest Date			
Control		Cell Path			
Fermentation Run ID		Cell Banking ID			
Cell Line		E. Coli Strain			
Expression Media		Days Incubated 3			
Growth Factors		Transfection Date			
Supplements		Transfer Date			
Warning		Transfer Volume 1liter(s)			
Gels		PUBIS PUR1039 11/23/98			
Expressed		TRUE			
Comments					
Status					
Date Entered		November 9, 1998		Date Complete	
Date Canceled				Cancel Reason	
Scientist		Bethanne Deuel		Status	
Notebook		0 -		Storage Location	
Protein Lots					
No LOTs for this EXPression					

ASY | DNA | DOM | EXP | FAM | FLS | LIB | LOT | MAP | OLI | PRO | PUR | RNA | SRC | UNQ | XPI | YST
 Assay Viewer | Sequence Viewer | Gene Viewer | GeneGenes | SAGE

GeneGenes Feedback

Appl. No. : 10/036,041
 Filed : December 26, 2001

EXHIBIT B—PAGE 4

GENEN GENES		SITE MAP		Additional f	
GENE VIEWER SEQUENCE VIEWER ASSAY VIEWER		GENE FAM MAP GENEHUB SRC RNA LIB FLS OLI EXP PUR LOT ASY		SELECT <input type="text"/> Go	
EXP2794		VIEW DNA		Copy Protein	
Gene Info		UNQ753 PRO 4365 Human CTRP3 Poly-His TFDNA102368 FLDNA44686			
EXP Lab Name		sst.44686.H8			
DNA Lab Name		sst.44686.H8			
Protein Request ID					
System		Mammalian Stable			
Expctd. Harvest Date		Harvest Date			
Control		Cell Pellet			
Fermentation Run ID		Cell Banking ID			
Cell Line		CHO			
Expression Media		E. coli Supernatant			
Growth Factors		# Days Incubated			
Supplements		Transfection Date February 17, 1999			
Warning		Transfer Date			
Gels		Transfer Volume			
		PURE			
Expressed		FALSE			
Comments		no band on western			
Status					
Date Entered		February 16, 1999		Date Complete	
Date Canceled				Cancel Reason	
Scientist		Lhney Lewis-Steiner		Status Drop	
Notebook		30966 - 55		Storage Location Crowley Lab	
Protein Lots					
No LOTs for this EXPression					
ASY DNA DOM EXP FAM FLS LIB LOT MAP OLI PRB PRO PUR RNA SRC UNQ XPT YST Assay Viewer Sequence Viewer Gene Viewer GenenGenes SAGE					
GenenGenes Feedback					

Appl. No. : **10/036,041**
Filed : **December 26, 2001**

EXHIBIT C

(2 pages; pages 26-27)

Appl. No. : 10/036,041
 Filed : December 26, 2001

EXHIBIT C—PAGE 1

GENEN GENES		SITEMAP		Additional F	
GENEVIEWER GENE FAM MAP GENENUE7 SEQUENCE VIEWER DNA SRC RNA UB FLS OLI ASSAY VIEWER PRS DOM EXP PUR LOT ASY		SELECT <input type="text"/> Go			
PUR1009		View DNA View Protein Update Record			
Gene Info UNQ753 PRO 1825 Human CTRP3 Poly-His TF DNA84665 FL DNA44686					
Protein Request ID					
DNA Lab Name		pE44686-1			
PUR Name		Protein Form Name			
Export PUR Date		Control			
EXP EXP2247		PUR Date July 13, 1999			
Mass Spec		No Sequence Report Available			
Warning		Sequence Info			
Endotoxin Level 6.24 EU/ml		GELS GEL461			
ELIS Molar Mass (g/mol)		AX Analysis (mg/ml)			
Endo Coef. (mg/ml) (cm)		OD 280			
Protein (mg/ml)		Endotoxin Units/mg Protein			
Reduced SDS MW Approx. 31, 55 kDa		Prior A ppm			
Theoretical MW of ORF (kDa) 26723.56					
Gel Score					
Buffer 1 mM HCl / 0.15 M NaCl / 4% mannitol					
Comments					
Status					
Date Entered November 16, 1998		PUR Done Date			
Yield Concentration 4752 nM		Yield Volume 4.5ml			
Date Canceled		Cancel Reason			
Scientist Corpuz, Racquel		Status Done			
Delivered To		Origin			
Notes 32647-8-		Storage Location			
Protein Lots					
OT2552		PIN1308-1		1009	

[ASY](#) | [DNA](#) | [DOM](#) | [EXP](#) | [FAM](#) | [FLS](#) | [UB](#) | [LOT](#) | [MAP](#) | [OLI](#) | [PRS](#) | [PRO](#) | [PUR](#) | [RNA](#) | [SRC](#) | [UNQ](#) | [XPT](#) | [YST](#)
[Assay Viewer](#) | [Sequence Viewer](#) | [Gene Viewer](#) | [GenenGenes](#) | [SAGE](#)

[GenenGenes Feedback](#)

Appl. No. : 10/036,041
Filed : December 26, 2001

EXHIBIT C—PAGE 2

P121009

5/1/04 2:47 PM

GENE GENES										Additional Resources:																			
Find New Update																													
SELECT										Go																			
View DNA ss.										View Protein p1.										Update Record									

PUR1009

Gene Info UNQ753 PRO 1009 Human CTRP3 Poly-His TE DNA44685 FL DNA44686

Protein Request ID

DNA Lab Name pE44686-1

PUR Name

Expctd. PUR Date

EXP EXP2247

Mass Spec

Warning

Endotoxin Level 6.24 EU/ml

LLS Molar Mass (g/mol)

Ext.Cocf. (mg/ml)*¹(cm)⁻¹

Prot A ng/ml

Reduced SDS MW Approx. 31, 55 kDa

Theoretical MW of ORF#1 26723.56

Gel Score

Buffer 1 mM HCl / 0.15 M NaCl / 4% mannitol

Comments

Status

Date Entered November 16, 1998

Yield Concentration 4752 nM

Date Canceled

Scientist Comuz, Rastoul

Delivered To

Notebook 32647-8-

Protein Lots

PIN1308-1

1009

Protein Formalname

Control

PUR Date July 13, 1999

No Sequence report available

Sequence Info

GELS GEL461

AA Analysis(mg/ml)

OD 280

Endotoxin Units/mg Protein

Prot A ppm

PUR Done Date

Yield Volume 4.5ml

Cancel Reason

Status Done

Origin

Storage Location

LOT2852

ASY | DNA | DOM | EXP | FAM | FLS | LIB | LOT | MAP | QLI | PRB | PRO | PUR | RNA | SRC | UNQ | XPT | YST
Assay Viewer | Sequence Viewer | Gene Viewer | Gene Genes | SAGE

[GeneGenes Feedback](#)

Appl. No. : **10/036,041**
Filed : **December 26, 2001**

EXHIBIT D

(3 pages; pages 29-31)

EXHIBIT D—PAGE 1

-29-

Appl. No. : 10/036,041
 Filed : December 26, 2001

EXHIBIT D—PAGE 2

<u>ASY64</u>	Retired	11/4/99	12/14/99	Proinflammatory/PMN infiltrate
<u>ASY67</u>	Retired	9/2/99	9/28/99	MLR - Inhibitory
<u>ASY68</u>	On Hold	10/18/99	11/8/99	Hu Venous Endothelial Cell Ca Flux Assay
<u>ASY74</u>	Retired	9/28/99	11/8/99	Inhibition of Heart Neonatal Hypertrophy Induced by LIF+ET-1
<u>ASY75</u>	Retired	9/28/99	11/8/99	Enhancement of Heart Neonatal Hypertrophy Induced by LIF+
<u>ASY100</u>	Running	8/20/99		Endotoxin Level (LAL)
<u>ASY103</u>	Running	9/1/99		Protein Gel Analysis
<u>ASY106</u>	Retired	10/2/99	12/1/99	Glucose and FFA uptake in Differentiated Skeletal Muscle
<u>ASY106</u>	Retired	12/3/99	1/4/00	Glucose and FFA uptake in Differentiated Skeletal Muscle
<u>ASY107</u>	Running	11/16/99	1/4/00	Fetal hemoglobin induction in an erythroblastic cell line
<u>ASY110</u>	Retired	10/22/99	11/10/99	Chondrocytes Re-differentiation Assay
<u>ASY110</u>	Retired	12/1/99	4/5/00	Chondrocytes Re-differentiation Assay
<u>ASY110</u>	Retired	12/15/99	3/27/00	Chondrocytes Re-differentiation Assay
<u>ASY110</u>	Retired	5/2/00	8/18/00	Chondrocytes Re-differentiation Assay
<u>ASY110</u>	Retired	5/16/00	8/18/00	Chondrocytes Re-differentiation Assay
<u>ASY111</u>	Retired	10/22/99	11/10/99	Chondrocytes Proliferation Assay
<u>ASY111</u>	Retired	12/1/99	4/5/00	Chondrocyte Proliferation Assay
<u>ASY111</u>	Retired	12/15/99	3/27/00	Chondrocyte Proliferation Assay
<u>ASY111</u>	Retired	5/2/00	8/18/00	Chondrocyte Proliferation Assay
<u>ASY111</u>	Retired	5/16/00	8/18/00	Chondrocyte Proliferation Assay
<u>ASY118</u>	Retired	1/12/00	2/1/00	Inhibition of A -Peptide Binding to Factor VIIA
<u>ASY119</u>	Retired	1/12/00	2/1/00	Inhibition of A -Peptide Binding to Factor VIII
<u>ASY128</u>	Retired	5/5/00	6/20/00	Cytokine Release in Human Whole Blood
<u>ASY129</u>	Retired	5/16/00	8/18/00	Chondrocytes re-differentiation by Fluorescence
<u>ASY130</u>	Retired	5/16/00	8/18/00	Chondrocytes Proliferation by fluorescence
<u>ASY132</u>	Retired	6/23/00	8/7/00	Activation of NFkB
<u>ASY134</u>	Retired	10/13/00	11/30/00	Activatin of NfkB [Luciferase]
<u>ASY134</u>	Retired	12/5/00	1/22/01	Activatin of NfkB [Luciferase]
<u>ASY135</u>	Retired	9/12/00	10/19/00	Induction of E-selectin
<u>ASY138</u>	Running	2/23/01	4/9/01	Normal Human Iliac Artery Endothelial cells

Appl. No. : 10/036,041
 Filed : December 26, 2001

EXHIBIT D—PAGE 3

ASY139	Running	2/23/01	4/9/01	Pooled Human Umbilical vein Endothelial cells
ASY140	Running	2/23/01	4/9/01	Coronary artery Smooth Muscle cells
ASY141	Running	2/23/01	4/9/01	Normal human Dermal Fibroblast Proliferation
ASY142	Running	2/14/01	3/26/01	NF-kappa B Inhibition Assay
ASY142	Running	3/8/01	3/26/01	NF-kappa B Inhibition Assay
ASY146	Running	7/19/01	8/3/01	Human Microvascular Endothelial Cell Proliferation Assay
ASY162	Running	11/16/99	9/5/00	NCI Oncology Screen-1
ASY165	Running	8/1/01	9/19/01	CREB
ASY165	Running	9/19/01	9/24/01	CREB
ASY170	Piloting	11/9/01	11/16/01	NHEK proliferation assay
ASY174	Piloting	3/12/02	4/3/02	Bovine Retinal M Endothelial
ASY174	Piloting	4/4/02		Bovine Retinal M Endothelial
ASY174	Piloting	5/17/02		Bovine Retinal M Endothelial
ASY174	Piloting	11/20/02		Bovine Retinal M Endothelial
ASY175	Running	12/21/01		Neuronal Differentiation using Rinat technology
ASY175	Running	5/30/02		Neuronal Differentiation using Rinat technology
ASY176	Piloting	5/31/02		Hemoglobin Assay
ASY176	Piloting	7/16/02		Hemoglobin Assay
ASY177	Piloting	4/22/03	8/18/03	fibroblast migration assay
ASY178	Running	1/23/03		Proliferation of Fibroblasts
ASY180	Running	3/11/03	3/25/03	Mouse Keratinocyte Assay
ASY181	Running	3/6/03	3/13/03	Human Mammary Epithelial Cell Assay

ASY | RNA | DNA | DOM | EXP | FAM | FLS | LIB | LOT | MAP | OL | FRB | PRQ | PUR | RNA | SRC | MNQ | XPT | YST
 Assay Viewer | Sequence Viewer | Gene Viewer | GeneGates | SAGE

Genentech Feedback

Appl. No. : **10/036,041**
Filed : **December 26, 2001**

EXHIBIT E

(2 pages; pages 33-34)

EXHIBIT E—PAGE 1

GreenGames Feedback

EXHIBIT E—PAGE 2

-34-